

Application No. 10/069,018

Amendment dated October 1, 2003

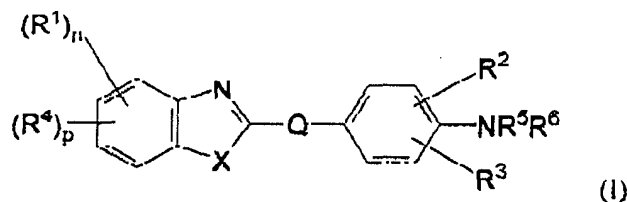
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Amendments to the Claims:

The following claims will replace all prior versions of the claims in this application (in the unlikely event that no claims follow herein, the previously pending claims will remain):

1-25. (Cancelled).

26. (New) An arylbenzazole compound represented by the structural formula I below, or a pharmaceutically acceptable salt thereof.



wherein

X represents S or O;

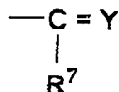
R¹ independently represents fluoro, iodo or trimethyltin;

R² represents hydrogen, NO₂, N₃, halogen, alkyl, a halo substituted or hydroxy substituted alkyl, CN or CF₃;

R³ represents hydrogen, halogen, alkyl, or a halo substituted or hydroxy substituted alkyl;

R⁴ independently represents alkyl, a halo substituted or hydroxy substituted alkyl, hydroxyl, alkoxy or aralkoxy;

R⁵ and R⁶ each independently represent hydrogen, an amino acid, an alkyl, or a group



wherein Y represents O or S, and R⁷ represents alkyl or -CH(R⁸)NH₂ where R⁸ represents hydrogen, or an optionally substituted alkyl,

Q represents a direct bond, CH₂ or -CH-CH-;

p represents zero, 1 or 2; and

n represents zero, 1, 2 or 3;

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subject to the following provisos:

- (a) alkyl or substituted alkyl groups include linear, branched or cyclic structures but when present as linear or branched structures in the compound or as a moiety in another group such as alkoxy they are composed of less than ten carbon atoms;
- (b) p represents zero or 1 when n represents 3;
- (c) when n represents zero, at least one of R⁵ or R⁶ represents -C(Y)-CH(R⁸)NH₂;
- (d) when a group is optionally substituted, unless otherwise specified, the substituent is selected from one or more of the following: a halogen, OH, SH, NH₂, COOH and CONH₂.

27. (New) An arylbenzazole compound of claim 26 with at least one the following features:

- (a) alkyl groups when present as such or as a moiety in other groups such as alkoxy each contain less than six carbon atoms;
- (b) at least some alkyl groups when present as such or as a moiety in other groups such as alkoxy are methyl or ethyl; or
- (c) halogen substituents, when present, are selected from fluorine, iodine, bromine and chlorine.

28. (New) An arylbenzazole compound of Claim 27 where the halogen substituent is fluorine.

29. (New) An arylbenzazole compound of Claim 29 wherein the compound incorporates the isotope ¹⁸F.

30. (New) An arylbenzazole compound of Claim 26 or 27 wherein R¹ is fluorine.

31. (New) An arylbenzazole compound of claim 26 wherein R¹ is in the 5-position of the benzazole moiety.

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32. (New) An arylbenzazole compound of claim 26 wherein R^2 is a substituent in the 3' position of the phenyl group.

33. (New) An arylbenzazole compound of claim 26 wherein X is sulphur.

34. (New) An arylbenzazole compound of claim 26 wherein one of R^5 and R^6 is $C(Y)-CH(R^8)NH_2$ or a salt thereof, and the other is hydrogen.

35. (New) An arylbenzazole compound of claim 26 wherein Y is O and R^6 is selected from hydrogen, $-CH_3$, $-(CH_2)_4NH_2$ or $-CH_2OH$.

36. (New) An arylbenzazole compound of Claim 26 or 27 wherein $p = 0$, R^5 and R^6 are both hydrogen, and the combination of substituents R^3 , X and R^2 is selected from one of the following combinations:

R^3	X	R^2
H	S	3'-Me
H	S	3'-Et
H	O	3'-I
H	S	3'-Br
H	S	3'-Cl
H	S	3'-CN
5'-Br	S	3'-Br
5'-Cl	S	3'-Cl
5'-Me	S	3'-Cl
H	S	3'-F

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37. (New) An arylbenzazole compound of Claim 26 or 27 wherein $p = 0$, X represents S, wherein R^3 , R^5 and R^6 each represent H, wherein Q represents a direct bond and wherein n, R^1 and R^2 represent one of the following combinations:

<u>n</u>	<u>R^1</u>	<u>R^2</u>
1	4-F	3-CH ₃
1	6-F	3-CH ₃
1	4-F	H
1	6-F	H
2	4,5-diF	3-CH ₃
2	4,6-diF	3-CH ₃
2	5,7-diF	3-CH ₃
1	7-F	3-CH ₃
2	5,6-diF	3-CH ₃
2	6,7-diF	3-CH ₃
1	5-F	3-CH ₃
1	5-F	H
1	4-F	3-I
1	5-F	3-I
1	6-F	3-I
1	4-F	3-Cl
1	5-F	3-Cl
1	6-F	3-Cl
1	4-F	3-Br
1	5-F	3-Br
1	6-F	3-Br

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38. (New) An arylbenzazole compound of Claim 26 or 27 wherein $p = 0$, X represents S, Q represents a direct bond, one of R^5 and R^6 represents H and the other represents -C(O)CH(R^8)NH₂, and wherein R^3 represents H, and n, R^1 , R^2 and R^8 represent one of the following combinations.

n	R^1	R^2	R^8
Zero	-	H	-CH ₃
Zero	-	3-ClI ₃	-CH ₃
Zero	-	3-Cl	CH ₃
Zero	-	H	-(CH ₂) ₄ NH ₂
Zero	-	3-CH ₃	-(CH ₂) ₄ NH ₂
Zero	-	3-Cl	-(CH ₂) ₄ NH ₂
Zero	-	3-CH ₃	-CH ₂ OH
1	6-F	3-CH ₃	-CH ₃
1	5-F	3-CH ₃	-(CH ₂) ₄ NH ₂
1	6-F	3-ClI ₃	-(CH ₂) ₄ NH ₂
1	5-F	3-CH ₃	CH ₃
1	5-F	3-CH ₃	H

39. (New) An arylbenzazole compound which is one of the following:

- 4 Fluoro-2-(4'-amino-3'-methylphenyl)benzothiazole;
- 6 Fluoro-2-(4'-amino-3'-methylphenyl)benzothiazole;
- 4 Fluoro-2-(4'-aminophenyl)benzothiazole;
- 6 Fluoro-2-(4'-aminophenyl)benzothiazole;
- 4,5-Difluoro-2-(4'-amino-3'-methylphenyl)benzothiazole;
- 4,6-Difluoro-2-(4'-amino-3'-methylphenyl)benzothiazole;
- 5,7-Difluoro-2-(4'-amino-3'-methylphenyl)benzothiazole;
- 7-Fluoro-2-(4'-amino-3'-methylphenyl)benzothiazole;
- 5,6-Difluoro-2-(4'-amino-3'-methylphenyl)benzothiazole;
- 6,7-Difluoro-2-(4'-amino-3'-methylphenyl)benzothiazole;

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5-Fluoro-2-(4'-amino-3'-methylphenyl)benzothiazole;
5-Fluoro-2-(4'-aminophenyl)benzothiazole,
4-Fluoro-2-(4'-amino-3'-iodophenyl)benzothiazole;
5-Fluoro-2-(4'-amino-3'-iodophenyl)benzothiazole;
6-Fluoro-2-(4'-amino-3'-iodophenyl)benzothiazole;
4-Fluoro-2-(4'-amino-3'-chlorophenyl)benzothiazole;
5-Fluoro-2-(4'-amino-3'-chlorophenyl)benzothiazole;
6-Fluoro-2-(4'-amino-3'-chlorophenyl)benzothiazole;
4-Fluoro-2-(4'-amino-3'-bromophenyl)benzothiazole;
5-Fluoro-2-(4'-amino-3'-bromophenyl)benzothiazole;
6-Fluoro-2-(4'-amino-3'-bromophenyl)benzothiazole,
2-(4'-Aminophenyl)benzothiazole alanyl amide hydrochloride salt;
2-(4'-Amino-3'-methylphenyl)benzothiazole alanyl amide hydrochloride salt;
2-(4'-Amino-3'-chlorophenyl)benzothiazole alanyl amide hydrochloride salt;
2-(4'-Aminophenyl)benzothiazole lysyl amide dihydrochloride salt;
2-(4'-Amino-3'-methylphenyl)benzothiazole lysyl amide dihydrochloride salt;
2-(4'-Amino-3'-chlorophenyl)benzothiazole lysyl amide dihydrochloride salt;
2-(4'-Amino-3'-methylphenyl)benzothiazole serine hydrochloride salt;
6-Fluoro-2-(4'-amino-3'-methylphenyl)benzothiazole alanyl amide hydrochloride salt;
5-Fluoro-2-(4'-amino-3'-methylphenyl)benzothiazole lysyl amide dihydrochloride salt;
6-Fluoro-2-(4'-amino-3'-methylphenyl)benzothiazole lysyl amide dihydrochloride salt;
5-Fluoro-2-(4'-amino-3'-methylphenyl)benzothiazole alanyl amide hydrochloride salt;
5-Fluoro-2-(4'-amino-3'-methylphenyl)benzothiazole glycyl amide hydrochloride salt;
5-Iodo-2-(4'-amino-3'-methylphenyl)benzothiazole;
7-Iodo-2-(4'-amino-3'-methylphenyl)benzothiazole;
5-Fluoro-2-(4'-acetamido-3'-methylphenyl)benzothiazole;
5-Fluoro-2-(4'-amino-3'-cyanophenyl)benzothiazole;
4-Fluoro-2-(4'-amino-3'-cyanophenyl)benzothiazole;
6-Fluoro-2-(4'-amino-3'-cyanophenyl)benzothiazole;

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5-Fluoro-2-(4'-amino-3'-(hydroxymethyl)phenyl)benzothiazole;
5,6-Difluoro-2-(4'-amino-3'-methylphenyl)benzothiazole alanyl amide hydrochloride salt;
5,6-Difluoro-2-(4'-amino-3'-methylphenyl)benzothiazole lysyl amide dihydrochloride salt; and
5-Trimethylstannyl-2-(4'-amino-3'-methylphenyl)benzothiazole.

40. (New) An arylbenzazole compound of claim 26 for use in therapy as an active therapeutic substance wherein said arylbenzazole compound is an acid addition salt derived from an acid selected from the group consisting of: hydrochloric, hydrobromic, sulphuric, nitric, phosphoric, maleic, salicylic, p-toluenesulphonic, tartaric, citric, lactobionic, formic, malonic, pantothenic, succinic, naphthalene-2-sulphonic, benzenesulphonic, methanesulphonic and ethanesulphonic.

41. (New) A isotopically labelled arylbenzazole compound selected from the group consisting of 5-¹⁸F-fluoro-2-(4'-amino-3'-methylphenyl)benzothiazole and 6-¹⁸F-fluoro-2-(4'-amino-3'-methylphenyl)benzothiazole.

42. (New) A pharmaceutical formulation for medical use comprising a compound of claim 26 and a pharmaceutically acceptable carrier.

43. (New) A medical preparation comprising: a therapeutically effective non-toxic amount of a compound of claim 26 and a pharmaceutically inert excipient.

44. (New) A unit dosage of a pharmaceutical preparation as an antitumour agent in treating mammals comprising a therapeutically-effective non-toxic amount of a compound of claim 26.

45. (New) A method of reducing or inhibiting cancer cell growth in a mammal comprising administering to said mammal an effective amount of an pharmaceutical formulation according to claim 42.

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46. (New) A method for the preparation of a compound as claimed in Claim 26 substantially as herein described in "Route E".

47. (New) A method as claimed in Claim 46 wherein the compound is an amino acid amide prodrug.